

Time and Temperature Profile of Catheter Cryoablation of Right Septal and Free Wall Accessory Pathways in Children

JONATHAN R. KALTMAN, M.D.,* RONN E. TANEL, M.D.,* BRADLEY WEGRZYNOWICZ,†
ERIC KOZODOY, R.N.,† TAMMY WIEAND, M.S.,* JEAN ENNIS, R.N.,*
VICTORIA L. VETTER, M.D.,* and MAULLY J. SHAH, M.B.B.S.*

From the *Division of Cardiology, The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA;
and †CryoCath Technologies Inc., Montreal, Quebec, Canada

Cryoablation of Accessory Pathways in Children. *Introduction:* The overall acute success with cryoablation for accessory pathways (APs) has been reported to be lower than with radiofrequency ablation. Generally, prior cryomapping (limited to -30°C) has been used to test for loss of AP conduction and absence of atrioventricular (AV) node impairment. However, the temperature at which loss of AP conduction occurs may be variable. The purpose of this study was to evaluate the time and temperature profile at which loss of AP conduction occurs.

Methods and Results: A retrospective study evaluated 25 patients (mean age 13.3 ± 3.6 years) who underwent cryoablation for right-sided APs (22 manifest/3 concealed). Direct cryoablation (-80°C) without cryomapping was performed using a "time to success" strategy. If AP conduction was successfully interrupted within 25 seconds of the onset of cryoablation, the lesion was continued for 240 seconds; otherwise it was terminated and further mapping was performed. Cryoablation was successful in 24/25 (96%) patients. Temperature at loss of AP conduction was $-66.2 \pm -16.7^{\circ}\text{C}$ (range $+32$ to -84°C) with conduction block at temperatures lower than -30°C for all but 3 APs. Critical time to success (interval from cryoadherence to loss of AP conduction) was significantly shorter for permanently successful cryolesions, compared with transiently successful lesions (6.3 ± 4.1 vs. 11.2 ± 2.2 sec; $P < 0.001$). There were no major complications.

Conclusions: Cryothermal energy required for successful ablation may be variable and restricting test applications to -30° may limit its efficacy. A "time to success" strategy may improve outcome of cryoablation for right-sided APs in children without compromising safety. (*J Cardiovasc Electrophysiol*, Vol. 19, pp. 343-347, April 2008)

cryoablation, accessory pathways, pediatrics

Cryoenergy has been shown to be a safe energy source for catheter ablation of accessory pathways (AP) and atrioventricular (AV) nodal reentrant tachycardias in pediatric patients.¹⁻⁶ An important advantage of cryoablation is the reversible tissue damage that it causes during progressive cooling.^{3,7} However, acute rates of successful interruption of APs have been lower than with radiofrequency energy.^{1,4} Also, recurrence rates after an acutely successful procedure have been higher.⁴

Previous reports have generally described a cryomapping approach in conjunction with a 4-mm tip cryoablation catheter.¹⁻⁵ Cryomapping involves cooling the catheter tip to -30°C to -35°C for up to 120 seconds at a prospective ablation site to test for loss of AP conduction and absence of AV nodal conduction impairment. If the expected result is obtained, then cryoablation at -70°C to -75°C is performed.

Permanence of tissue destruction with cryothermal energy is related to time-dependent variables and tissue temperature. Theuns *et al.* described successful cryomapping attempts as having a rapid cooling phase from onset of cryoenergy to the steady-state cryomapping temperature.⁸ However, the temperature at which loss of AP conduction occurs is not known and may be variable. There are multiple factors that affect tissue temperature and lesion size, including electrode size, tissue contact, catheter tip temperature, and convective warming.^{9,10}

There are limited data in the literature evaluating temperature profile and time-dependent variables during transcatheter cryoablation. Optimization of these variables may improve success rates of cryoablation. Therefore, the purpose of this study was to evaluate our recent experience with cryoablation of right-sided APs using a "time to success" cryoablation strategy and to assess the temperature profile and ablation-dependent variables at which loss of APs occurs.

B. Wegrzynowicz and E. Kozodoy are full-time employees of CryoCath Technologies Inc.

Address for correspondence: Jonathan Kaltman, M.D., Department of Cardiology, Children's National Medical Center, 111 Michigan Ave, N.W., Washington, D.C. 20010. Fax: 202-884-5700; E-mail: jkaltman@cnmc.org

Manuscript received 27 July 2007; Revised manuscript received 20 September 2007; Accepted for publication 19 October 2007.

doi: 10.1111/j.1540-8167.2007.01048.x

Methods

Patient Population

We performed a retrospective review of consecutive children and adolescents who underwent cryoablation for a right-sided AP from October 2005 to December 2006. Informed consent was obtained prior to undergoing the electrophysiology study and catheter ablation procedure. The study was approved by the local institutional review board.

Electrophysiology Study and Ablation

In the postabruptive state, the patients underwent a standard electrophysiology study under general anesthesia or conscious sedation. Multipolar electrode catheters were positioned at the high right atrium, His bundle position, right ventricular apex, and in the coronary sinus. Mapping of the AP confirmed a right-sided location and cryoablation was used as the primary ablation modality or following failed radiofrequency ablation attempts.

Cryoablation was performed using a 7 Fr 6-mm tip Freezor Xtra catheter (CryoCath Technologies Inc., Quebec, Canada) in all cases. Based partially upon industry recommendation and prior clinical experience with radiofrequency ablation, a "time to success" strategy was employed during cryoablation. Direct cryoablation to a target temperature of -80°C was performed without cryomapping (-30°C). If the AP was successfully interrupted within 25 seconds of the onset of cryoablation without compromise of AV node conduction, then the lesion was continued for 240 seconds. If success did not occur within 25 seconds, the lesion was terminated and the catheter was moved to another position. A cut-off time of 25 seconds was based empirically upon the radiofrequency ablation experience in which we use a 15-second cut-off for time to effect and to allow additional time for the delay in catheter cooling. Typically, additional cryolesions were placed, at the discretion of the operator, following the successful lesion as part of a freeze-thaw-freeze cycle. Patients were observed and repeat electrophysiology testing was performed for 60 minutes following the successful lesion in order to determine that a procedure was successful. Outpatient follow-up visits with electrocardiograms were scheduled for 1, 6, and 12 months following the procedure.

Data Reviewed

Charts were reviewed for patient demographic, procedural, and outcome variables. Procedural variables included:

Temperature profile parameters

Time delay: Interval from onset of cryoablation to catheter adherence (evidenced by distortion of local electrograms)⁸ (Fig. 1).

Temperature response time: Interval from onset of cryoablation to steady state of minimal catheter temperature⁸ (Fig. 1).

Ablation-dependent variables

Temperature at loss of AP: Recorded catheter tip temperature at the time when loss of AP conduction occurred.

Time to effect: Interval from onset of cryoablation to loss of AP conduction.

Critical time to effect: Interval from catheter adherence (evidenced by distortion of local electrograms) to loss of AP conduction.

Procedural data were obtained from successful cryolesions and from transiently successful cryolesions. Transiently successful cryolesions resulted in temporary interruption of AP conduction with recurrence of conduction during the procedure. Further mapping and cryoablation occurred after transiently successful lesions. Successful cryolesions resulted in permanent interruption of AP conduction. For patients with bidirectional conduction within the AP, elimination of both

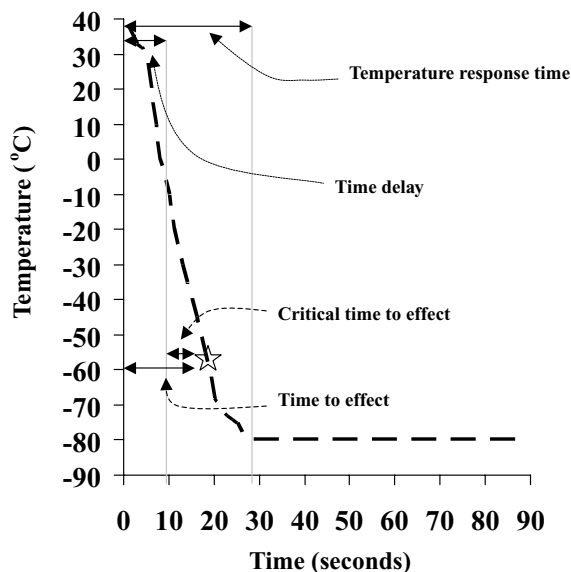


Figure 1. Temperature profile during cryoablation. Star represents time and temperature at which accessory pathway conduction is interrupted for a theoretical successful cryolesion. Definitions of time delay, temperature response time, time to effect, and critical time to effect are illustrated.

antegrade and retrograde conduction was confirmed before declaring a lesion successful.

Statistical Analysis

Continuous data are expressed as mean \pm standard deviation. Comparison of continuous variables was performed with Student *t*-tests. Comparison of proportions was performed with Fisher's exact test. A P-value of <0.05 was considered significant.

Results

Twenty-five patients (12 males/13 females) were enrolled in the study. The mean age at the time of procedure was 13.3 ± 3.6 years and mean weight was 50.4 ± 15.6 kg. All patients but one had structurally normal hearts. One patient had Ebstein's anomaly. Four (16%) patients had a prior electrophysiology study with failed radiofrequency ablation attempt.

The procedure was performed under general anesthesia in 14 (56%) patients. Manifest preexcitation was present in 22 (88%) patients, while 3 (12%) patients had concealed APs. APs were mapped to the anteroseptal region ($n = 9$, 36%), midseptal region ($n = 5$, 20%), free wall ($n = 4$, 16%), posterior septal region ($n = 3$, 12%), posterior region ($n = 2$, 8%), and proximal coronary sinus ($n = 2$, 8%).

In five procedures, radiofrequency ablation was unsuccessfully attempted prior to cryoablation. In these procedures, indications for transitioning to cryoablation was inadequate power generation with radiofrequency catheter ($n = 2$), catheter instability on AV groove despite the use of a long sheath ($n = 1$), pain with radiofrequency application ($n = 1$), and failure with radiofrequency energy ($n = 1$). In the procedures in which cryoablation was the only modality used ($n = 20$), indications for cryoablation included proximity to the AV node ($n = 16$), pathway location within the coronary sinus ($n = 1$), and catheter stability ($n = 3$). Three

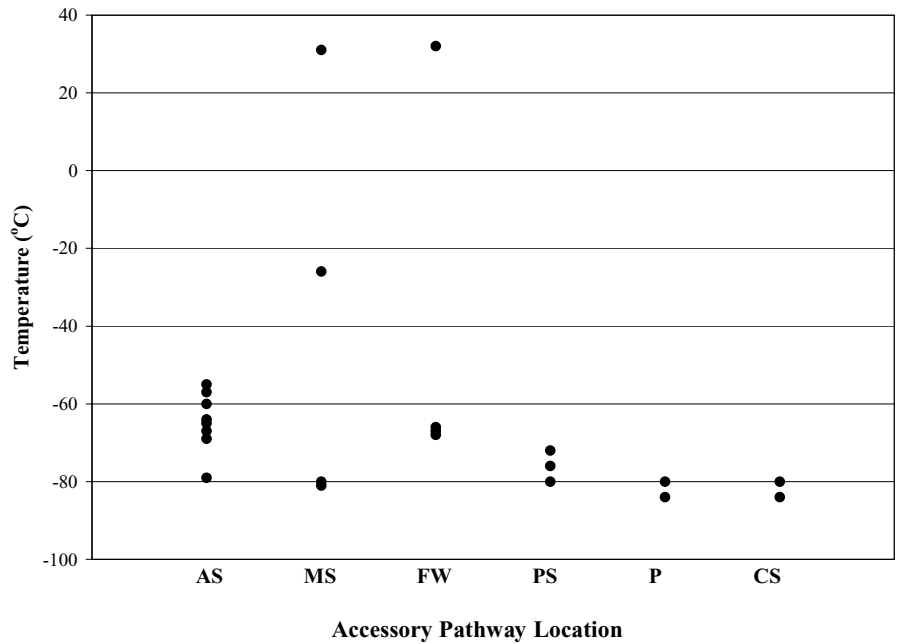


Figure 2. Temperature at the time of loss of accessory pathway conduction by pathway location. AS = anteroseptal; FW = free wall; MS = midseptal; PS = posteroseptal; P = posterior; CS = coronary sinus.

of these patients had undergone a prior failed procedure in which radiofrequency ablation was attempted.

The mean total number of cryoablation lesions per procedure was 7.4 ± 4.5 (range 2–20). The mean total duration of cryothermal energy application at the site of successful elimination of AP conduction was 593 ± 316 seconds (range 240–1440 seconds). This included the initial successful lesion plus an additional median of 1 (range 0–5) lesions. The mean procedure duration was 185 ± 69 minutes.

Cryoablation was acutely successful in 24 of 25 procedures (96%). For all patients with manifest preexcitation, a single cryolesion eliminated both antegrade and retrograde conduction. The failed procedure involved a midseptal AP. Pathway conduction was eliminated within 3 seconds of onset of cryothermal energy application, but was immediately followed by transient third degree AV block. The procedure was subsequently aborted. During a mean follow-up (interval from procedure to last cardiology clinic visit) of 7.6 ± 3.8 months, there was one recurrence (4%), giving a 92% overall mid-term success rate after a single cryoablation procedure. Eighteen of 24 (75%) patients have had follow-up of greater than 6 months.

The one recurrence involved a concealed anteroseptal AP which was mapped during tachycardia to the earliest retrograde activation. Tachycardia terminated in a retrograde manner with catheter placement at the site of earliest activation. Mechanical termination of AP conduction was assumed and cryoablation was initiated immediately. At the end of the case, there was no inducible tachycardia and there was ventriculoatrial block with adenosine. Three months following the procedure the patient had a recurrence of tachycardia. The patient had a repeat successful cryoablation and has had no recurrence after 8 months.

There were two procedure-related complications (8%). One involved transient AH prolongation during cryoablation of a midseptal pathway. That procedure was successfully completed. The second complication involved transient third degree heart block during cryoablation of a midseptal AP (as described previously). That procedure was aborted.

Temperature Profile Parameters

The mean steady state cryoablation temperature was $-81.8 \pm 1.8^\circ\text{C}$ (range -80 to -86°C). For successful cryolesions, the mean time delay was 9.2 ± 0.9 seconds (range 8–11 seconds). For successful cryolesions, the mean temperature response time was 19.4 ± 3.8 seconds (range 15–29 seconds).

Ablation-Dependent Variables

The mean temperature at loss of the AP was $-66.2 \pm 16.7^\circ\text{C}$ (range $+32$ to -84°C). All but three APs were eliminated at temperatures less than -30°C (Fig. 2).

The mean time to effect was 15.5 ± 4.1 seconds (range 11.0–26.7 seconds). The mean critical time to effect was 6.3 ± 4.1 seconds (range 1.8–16.7 seconds). A critical time to effect of less than 10 seconds was observed in 87% of successful cryoablations (Fig. 3).

Transiently Successful Cryolesions

In seven patients, there were 19 transiently successful cryolesions (median two cryolesions per patient; range one to nine lesions). Characteristics of these transiently successful lesions and comparisons of these characteristics to those from permanently successful cryolesions are shown in Table 1. Compared with permanently successful lesions, only 3 of 19 (16%) transiently successful lesions had critical times to the effect of less than 10 seconds (87% vs. 16%; $P < 0.001$).

Discussion

Our experience with cryoablation of right-sided APs highlights several important findings. These include: (1) the temperature at AP elimination is variable and frequently lower than the typical cryomapping temperature of -30°C ; (2) successful cryolesions are characterized by short critical times to effect (preferably less than 10 seconds) and short time delays and temperature response times; and (3) a “time to success”

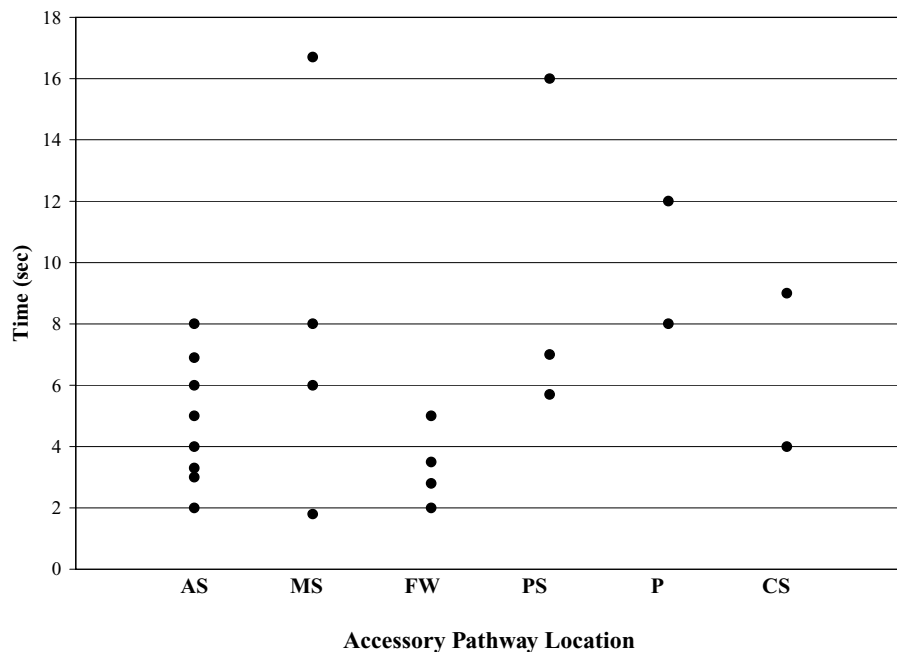


Figure 3. Critical time to effect by pathway location. AS = anteroseptal; FW = free wall; MS = midseptal; PS = posteroseptal; P = posterior; CS = coronary sinus.

strategy without cryomapping, using a 7 Fr 6-mm tip cryoablation catheter, can achieve a high chronic success rate with an adequate safety profile.

Previous pediatric studies have demonstrated acute procedural success rates for cryoablation of APs ranging from 60 to 83%,^{1-4,6} with one study citing a 95% success rate.⁵ Recurrence rates have been documented from 13 to 45%.¹⁻⁶ In a recent report documenting a multicenter experience of cryoablation of APs in the coronary sinus, Collins *et al.* report a 71% procedural success rate and a recurrence rate of 40%.¹¹ Comparatively, success rates of 88–93% have been achieved with radiofrequency ablation of right-sided APs with recurrence rates of 15–24%.^{12,13} Prior cryoablation studies employed a cryomapping strategy during which the catheter tip temperature was lowered to -30°C or -35°C for up to 120 seconds and AP conduction was assessed.¹⁻⁶ If AP conduction was eliminated, then cryoablation was performed with the catheter tip temperature further lowered to -70 to -75°C for 4 minutes. If AP conduction was not eliminated within the defined time range, the catheter was repositioned. Also, in the majority of the cited procedures, a 4-mm tip cryoablation catheter was used.

The finding from our study that catheter tip temperature varies considerably at AP elimination may provide one po-

tential explanation for the lower success rates and higher recurrence rates of cryoablation in these previous reports. Cryoablation lesion size is related to catheter tip temperature among other variables.^{9,10} In addition, catheter temperature determines the minimum freezing temperature of the contacted tissue. Limiting temperature to -30°C or -35°C during cryomapping may result in insufficient tissue damage or lesion volume to eliminate the AP. Additional supporting evidence for this hypothesis is provided by two observations. The first is that cryoablation can be successful at negative cryomapping sites. Kriebel *et al.*² reported that in 4 of 13 (31%) patients with an AP, cryoablation was performed at a site of unsuccessful cryomapping (because of compelling electrophysiology findings) and resulted in permanent interruption of the AP. The second observation, as documented by several groups,^{2,14,15} is that the cryoablation can cause impairment of AV node conduction at sites where cryomapping demonstrated no adverse effects.

Cryoablation lesion size is related not only to catheter temperature but also to time intervals necessary to cool the catheter to the target temperature and to rewarm the catheter.¹⁰ These time intervals are dependent upon electrode orientation, contact pressure, and convective warming and thus are surrogates for optimal electrode position and contact with the endocardium. Theuns *et al.*⁸ showed that the temperature response time was significantly shorter during successful ice mapping attempts, compared with unsuccessful attempts (35.8 ± 4.5 vs. 53.5 ± 11.0 seconds; $P < 0.001$). Our data demonstrated even brisker temperature response times during successful cryoablation lesions (always less than 30 seconds). However, no significant difference could be detected for temperature response time between permanently and transiently successful cryolesions. Our study did show a significantly shorter time delay for permanently successful cryolesions, compared with transiently successful ones. These data suggest the importance of catheter orientation and position during cryoablation.

We used a “time to success” strategy during cryoablation. Others have noted that rapidity of conduction block in the AP

TABLE 1

Characteristics of Transiently Successful Cryolesions and Comparison to Permanently Successful Cryolesions

	Transiently Successful Cryolesion	Permanently Successful Cryolesion	P-value
N	19	24	
Time delay (sec)	10.2 ± 1.5	9.2 ± 0.9	0.012
Temperature response time (sec)	17.8 ± 3.0	19.4 ± 3.8	0.157
Temperature at loss of AP ($^{\circ}\text{C}$)	-75.5 ± 5.0	-66.2 ± 16.7	0.018
Critical time to effect (sec)	11.2 ± 2.2	6.3 ± 4.1	<0.001

AP = accessory pathway.

is associated with long-term success.^{3,8} In our study, we show that the critical time to effect was significantly shorter for permanently successful cryolesions, compared with transiently successful cryolesions. In addition, the temperature at loss of AP conduction was lower for transiently successful lesions, compared with permanently successful ones. Cryolesions expand as the tissue temperature decreases with time. Thus, a longer critical time to effect coupled with a lower catheter tip temperature suggests a farther distance that the leading edge of the freeze zone must progress before encountering the AP. In these boundary regions of the cryolesion, tissue may not be as hypothermic as tissue closer to the catheter tip resulting in only transient electrical effects.¹⁵ This suggests that catheter tip proximity to the AP (i.e., pathway well within the freeze zone) is crucial for permanent interruption of AP conduction.

Our approach of cryoenergy ablation involved performing direct cryoablation for approximately 25 seconds from onset of cryoablation. If AP conduction block occurred within this time frame, the cryolesion was continued. If conduction block did not occur, the catheter was repositioned. With this approach, we achieved an acute procedural success rate (96%) and recurrence rate (4%) comparable with those achieved with radiofrequency ablation.^{12,13} Also, the safety profile of the “time to success” approach was similar to that seen using a cryomapping approach.¹⁻⁶

Limitations

It should be noted, though, that there are other important differences between our approach and the approach outlined in the previous reports. These differences include use of a 6-mm tip cryoablation catheter (rather than a 4-mm tip catheter) and the application of additional lesions in a freeze-thaw-freeze cycle. From our data, due to the lack of stratification of these variables (“time to success” approach, 6-mm tip catheter, and additional lesions), it is impossible to determine which of these variables is responsible individually or collectively for the success of our approach. In addition, our cohort consisted of more septal APs than freewall pathways. Thus, the findings of this study may be more applicable to septal APs. Other limitations of this study include its retrospective nature and small sample size.

Conclusion

We conclude that a “time to success” ablation strategy without cryomapping can achieve a high chronic success rate for cryoablation of right-sided APs with an adequate safety profile. This strategy takes into account the variability in temperature at which AP conduction block is observed. Important characteristics of a successful cryoablation lesion include a short critical time to effect (preferably less than 10 seconds), a short time delay, and a rapid temperature response time. These time and temperature related variables may indicate

optimal electrode orientation, tissue contact, and proximity to the AP. Failure to achieve these parameters may suggest the need for further mapping in order to achieve long-term success.

References

1. Kirsh JA, Gross GJ, O'Connor S, Hamilton RM: Transcatheter cryoablation of tachyarrhythmias in children. *J Am Coll Cardiol* 2005;45:133-136.
2. Kriebel T, Broistedt C, Kroll M, Sigler M, Paul T: Efficacy and safety of cryoenergy in the ablation of atrioventricular reentrant tachycardia substrates in children and adolescents. *J Cardiovasc Electrophysiol* 2005;16:1-7.
3. Miyazaki A, Blaufox AD, Fairbrother DL, Saul JP: Cryo-ablation for septal tachycardia substrates in pediatric patients. *J Am Coll Cardiol* 2005;45:581-588.
4. Bar-Cohen Y, Cecchin F, Alexander ME, Berul CI, Triedman JK, Walsh EP: Cryoablation for accessory pathways located near normal conduction tissues or within the coronary venous system in children and young adults. *Heart Rhythm* 2006;3:253-258.
5. Drago F, Silvetti S, De Santis A, Grutter G, Andrew P: Lengthier cryoablation and a bonus cryoapplication is associated with improved efficacy for cryothermal catheter ablation of supraventricular tachycardias in children. *J Interv Card Electrophysiol* 2006;16:191-198.
6. Papez AL, Al-Ahdab M, Dick M, Fischbach PS: Transcatheter cryotherapy for the treatment of supraventricular tachyarrhythmias in children: A single center experience. *J Interv Card Electrophysiol* 2006;15:191-196.
7. Friedman PL, Dubuc M, Green MS, Jackman WM, Keane DT, Marinchak RA, Nazari J, Packer DL, Skanes A, Steinberg JS, Stevenson WG, Tchou PJ, Wilber DJ, Worley SJ: Catheter cryoablation of supraventricular tachycardia: Results of the multicenter prospective “frosty” trial. *Heart Rhythm* 2004;1:129-138.
8. Theuns DA, Kimman GP, Szili-Torok T, Res JC, Jordaens LJ: Ice mapping during cryothermal ablation of accessory pathways in WPW: The role of the temperature time constant. *Europace* 2004;6:116-122.
9. Wood MA, Parvez B, Ellenbogen AL, Shaffer KM, Goldberg SM, Gaspar MP, Arief I, Schubert CM: Determinants of lesion size and tissue temperatures during catheter cryoablation. *Pacing Clin Electrophysiol* 2007;30:644-654.
10. Parvez B, Goldberg SM, Pathak V, Schubert CM, Wood MA: Time to electrode rewarming after cryoablation predicts lesions size. *J Cardiovasc Electrophysiol* 2007;18:845-848.
11. Collins KK, Rhee EK, Kirsh JA, Cannon BC, Fish FA, Dubin AM, Van Hare GF: Cryoablation of accessory pathways in the coronary sinus in young patients: A multicenter study from the pediatric and congenital electrophysiology society's working group on cryoablation. *J Cardiovasc Electrophysiol* 2007;18:592-597.
12. Van Hare GF, Javitz H, Carmelli D, Saul JP, Tanel RE, Fischbach PS, Kanter RJ, Schaffer M, Dunnigan A, Colan S, Serwer G: Prospective assessment after pediatric cardiac ablation: Demographics, medical profiles, and initial outcomes. *J Cardiovasc Electrophysiol* 2004;15:759-770.
13. Van Hare GF, Javitz H, Carmelli D, Saul JP, Tanel RE, Fischbach PS, Kanter RJ, Schaffer M, Dunnigan A, Colan S, Serwer G: Prospective assessment after pediatric cardiac ablation: Recurrence at 1 year after initially successful ablation of supraventricular tachycardia. *Heart Rhythm* 2004;1:188-196.
14. Fischbach PS, Saarel EV, Dick M: Transient atrioventricular conduction block with cryoablation following normal cryomapping. *Heart Rhythm* 2004;1:554-557.
15. Gaita F, Riccardi R, Hocini M, Haissaguerre M, Giustetto C, Jais P, Grossi S, Caruzzo E, Bianchi F, Richiardi E: Safety and efficacy of cryoablation of accessory pathways adjacent to the normal conduction system. *J Cardiovasc Electrophysiol* 2003;14:825-829.